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# Retinal Artery Changes Correlated with other Hypertensive Parameters in a Coronary Heart Disease Case-history Study

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We have been conducting a retrospective or case-history study of patients with coronary heart disease in an attempt to identify aetiological or "risk" factors. A retrospective study of this nature suffers from a number of defects (Bronte-Stewart and Krut, 1962; Mulcahy, 1967), and among these is the problem of the modification or alteration of patients' measurements or attributes by the development of overt disease or by subsequent hospitalization and treatment.

One attribute that may be altered is the patient's blood pressure. In particular we are aware that cardiac infarction may temporarily or permanently reduce the subject's basal systolic and diastolic pressure. In general this is a fairly immediate effect, and while such lowering of blood pressure is commonest in patients with extensive infarction, it is by no means invariable or confined to this group.

The modifying effect of cardiac infarction on blood pressure may interfere with the proper appreciation of the association between hypertension and coronary heart disease in a case-history study. This difficulty does not arise in untreated patients with other coronary syndromes, including acute coronary insufficiency and angina pectoris. Our case-history experience of the blood pressure status of patients with coronary heart disease has been previously reported (Mulcahy, Hickey, and Maurer, 1967).

In an attempt to overcome the difficulties created by the modifying effect of cardiac infarction on blood pressure, we have been measuring other possible or accepted parameters of hypertension and hypertensive disease in our patients. These other parameters include: (1) hypertensive changes in the retinal vessels; (2) hypertensive changes in the electrocardiogram; (3) heart size as measured by the cardiothoracic ratio; (4) the diameter of the thoracic aorta; and (5) a previous history of hypertension.

We hope ultimately to examine these different parameters and to identify correlations between them which may establish the usefulness of individual or of various combinations of measurements in retrospectively assessing the subject's pre-illness blood pressure status.

The purpose of this communication is to examine correlations between retinal artery changes and other parameters measured, including the systolic and diastolic blood pressure of patients. Certain changes in the retinal vessels have been established as being important indicators of the presence and severity of high blood pressure (Keith, Wagener, and Barker, 1939; Shelburne, 1965; Breslin *et al.*, 1966; Stokoe and Turner, 1966).

## Subjects and Methods

Two hundred and twenty patients with classical coronary heart disease or allied syndromes are included in this study. Their ages range from 29 to 59 years, with a mean age of 50. The study was confined to patients under 60 years, because, in a retrospective survey, younger people make more satisfactory and reliable subjects for a variety of reasons (Mulcahy and Hickey, 1966). In addition, involutionary changes do take place in the retinal vessels of older subjects which may be difficult to distinguish from hypertensive changes (Wertheim and Deming, 1955; Shelburne, 1965).

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The 220 subjects were divided into two groups. The 108 subjects in Group 1 suffered from past or recent cardiac infarction, established by certain rigid criteria of electrocardiogram, enzyme, and other changes (Mulcahy and Hickey, 1966). The 112 patients in Group 2 were evenly divided between acute coronary insufficiency and angina pectoris, but this group included 6 subjects who were investigated for peripheral vascular disease. The diagnosis of acute coronary insufficiency and angina pectoris was based on previously reported criteria (Mulcahy and Hickey, 1966).

*Assessment of Retinal Artery Changes.* Because of the notorious effect of observer bias on the assessment of hypertensive changes in retinal vessels, findings were reported by a trained observer who was unaware of the subject's blood pressure status and of the other attributes being measured. No subject was included where the blood pressure status was known to the observer beforehand.

Segmental constriction of the arteries and arteriovenous narrowing were accepted as significant changes of hypertension. Haemorrhages, exudates, and papilloedema were also accepted, but the frequency of these changes in a coronary population is very low. Hard, isolated exudates, in the absence of the above-mentioned arterial changes, were ignored. Isolated arteriovenous nicking close to the disk edge was not considered significant (Shelburne, 1965). Diffuse narrowing of the arteries with or without silver wiring was recorded in a special category, though other authors (Shelburne, 1965; Breslin *et al.*, 1966; Stokoe and Turner, 1966) do not consider these changes as important indicators of hypertension. Like others we had difficulty in measuring diffuse narrowing of the retinal vessels. Breslin *et al.* (1966) showed a close relation between segmental rather than diffuse narrowing of the arteries with raised diastolic blood pressure.

The fundal changes were separated into the following six grades.

*Grade I:* normal.
*Grade II:* slight narrowing of the arteries and increase in light reflex. (This Grade is borderline or doubtful.)
*Grade III:* definite narrowing and increase of light reflex.
*Grade IV:* early arteriovenous compression and irregularities of arterial lumen.
*Grade V:* marked arteriovenous compression and irregularities of arterial lumen.
*Grade VI:* haemorrhages and exudates with or without papilloedema.

Because of the small number of patients included in Grade VI, patients in Grade V and VI were grouped together for the purpose of this study.

*Systolic and Diastolic Blood Pressure.* All subjects were studied in hospital. The mean of four or more systolic and diastolic readings noted on the fourth day of hospitalization, before hypertensive treatment was started, when indicated, were recorded as the patients' basal blood pressure levels.

*Electrocardiogram.* Hypertensive changes were defined in the following four grades:

*Grade I:* normal.
*Grade II:* doubtful or borderline.
*Grade III:* left axis deviation, or maximum S+maximum R in chest leads greater than 4·5 cm. or characteristic S–T sag with flat or inverted T wave over the left ventricle.
*Grade IV:* characteristic S–T sag and T wave changes with left axis deviation and/or maximum S+maximum R in chest leads greater than 4·5 cm.

Left axis deviation is accepted with a frontal plane axis of −30 degrees or less.

*Heart Size.* Heart size was measured from a conventional six foot postero-anterior chest *x*-ray, and was expressed as a ratio of the maximum transverse heart diameter to the maximum internal thoracic cage diameter (Wood, 1956).

*Width of Thoracic Aorta.* This was measured from a conventional six-foot postero-anterior film. It is the transverse distance in mm. between the extreme right border of the ascending aorta and the extreme left border of the arch or descending aorta. In practice it is difficult in most cases to identify precisely the border of the ascending aorta.

*Previous History of Hypertension.* A history of hypertension was accepted if the patient had been previously treated for high blood pressure, if abnormal figures were available from previous hospital admissions, or if the patient had been rejected for life insurance or the Services because of high blood pressure.

## Results

The systolic and diastolic blood pressures of the patients were correlated and shown to be very close. The correlation coefficient for Group 1 patients (cardiac infarction) was 0·8654, while the coefficient for Group 2 patients (acute coronary insufficiency and angina pectoris) was 0·9096. The correlation coefficient for the whole group was 0·8921. The slightly poorer correlation between systolic and diastolic blood pressure in the infarct group may reflect a variable effect of infarction on the two levels of blood pressure.

*Fundi and Systolic Blood Pressure.* Tables I and II show the mean systolic blood pressure of patients with and without infarction in the different fundal groups. Table I shows that a significant difference exists only between grades I–IV and V+VI. No significant systolic blood pressure changes can be

TABLE I

SYSTOLIC BLOOD PRESSURE RELATED TO HYPERTENSIVE CHANGES IN RETINAL ARTERIES
(Group 1, cardiac infarction)

| | Fundal grade | | | | | Total |
|---|---|---|---|---|---|---|
| | I | II | III | IV | V+VI | |
| No. of patients | 31 | 22 | 18 | 24 | 13 | 108 |
| Mean blood pressure (mm. Hg) | 126·48 | 125·45 | 133·33 | 133·00 | 150·46 | 131·79 |
| SD | ±15·20 | ±33·20 | ±17·49 | ±20·96 | ±27·02 | ±22·91 |
| SE of mean | ±4·117 | ±4·887 | ±5·402 | ±4·679 | ±6·357 | ±2·205 |

Difference between groups (I–IV) and (V+VI) significant. ($0·01 < p < 0·05$) ($F = 3·02$ on 4 and 103 d.f.)

TABLE II

SYSTOLIC BLOOD PRESSURE RELATED TO HYPERTENSIVE CHANGES IN RETINAL ARTERIES
(Group 2, non-infarction group)

| | Fundal grade | | | | | Total |
|---|---|---|---|---|---|---|
| | I | II | III | IV | V+VI | |
| No. of patients | 41 | 14 | 20 | 23 | 14 | 112 |
| Mean blood pressure (mm. Hg) | 123·76 | 138·93 | 133·00 | 144·91 | 184·43 | 139·23 |
| SD | ±15·04 | ±16·19 | ±18·17 | ±16·63 | ±33·70 | ±19·22 |
| SE of mean | ±3·003 | ±5·139 | ±4·300 | ±4·000 | ±5·139 | ±1·817 |

$p < 0·01$ ($F = 27$ on 4 and 107 d.f.) Significant differences exist between Grades I and II; between III and IV; between IV and V+VI.

TABLE III

DIASTOLIC BLOOD PRESSURE RELATED TO BLOOD PRESSURE CHANGES IN RETINAL ARTERIES
(Group 1, cardiac infarction)

| | Fundal grade | | | | | Total |
|---|---|---|---|---|---|---|
| | I | II | III | IV | V+VI | |
| No. of patients | 31 | 22 | 18 | 24 | 13 | 108 |
| Mean blood pressure (mm. Hg) | 78·06 | 78·77 | 87·44 | 79·67 | 94·46 | 82·85 |
| SD | ±9·68 | ±14·77 | ±12·99 | ±12·74 | ±18·33 | ±14·09 |
| SE of mean | ±2·74 | ±3·25 | ±3·11 | ±4·27 | ±5·09 | ±1·26 |

$p = 0·01$ ($F = 3·64$ on 4 and 103 d.f.)

TABLE IV

DIASTOLIC BLOOD PRESSURE RELATED TO BLOOD PRESSURE CHANGES IN RETINAL VESSELS
(Group 2, non-infarction group)

| | Fundal grade | | | | | Total |
|---|---|---|---|---|---|---|
| | I | II | III | IV | V+VI | |
| No. of patients | 41 | 14 | 20 | 23 | 14 | 112 |
| Mean | 73·05 | 85·36 | 83·5 | 92·17 | 109·29 | 86·28 |
| SD | ±7·5 | ±9·3 | ±9·47 | ±7·51 | ±16·74 | ±14·41 |
| SE of mean | ±1·57 | ±1·27 | ±2·26 | ±2·11 | ±2·71 | ±1·36 |

$p < 0·01$ ($F = 29·47$ on 4 and 107 d.f.)

noted between the first four fundal categories. On the other hand, data from the non-infarction group (Table II) show a progressive rise in the mean systolic blood pressure according to the changes noted in the fundi. The poor correlation trend in the infarct group may possibly be attributed to the effect of the heart attack on the blood pressure.

*Fundi and Diastolic Blood Pressure.* There is also a significant correlation between the different retinal artery groups and the mean diastolic blood pressure of patients with and without infarction, but again the association is clearer in the case of the non-infarction group (Tables III and IV).

*Fundi and Electrocardiographic Changes.* Table V shows that there is a poor correlation between retinal vessel and electrocardiographic changes in patients with cardiac infarction, but there is a highly significant correlation present in the non-infarct group

TABLE V

RETINAL ARTERY CHANGES RELATED TO HYPERTENSIVE CHANGES IN ELECTROCARDIOGRAM
(Group 1, cardiac infarction)

| Electrocardiogram grade | Fundal grade | | | | | Total |
|---|---|---|---|---|---|---|
| | I | II | III | IV | V+VI | |
| I+II (negative or doubtful) | 27 | 17 | 9 | 18 | 8 | 79 |
| III+IV (positive) | 4 | 5 | 9 | 6 | 5 | 29 |
| Total | 31 | 22 | 18 | 24 | 13 | 108 |

$0 \cdot 10 > p > 0 \cdot 05$.

TABLE VI

RETINAL ARTERY CHANGES RELATED TO HYPERTENSIVE CHANGES IN ELECTROCARDIOGRAM
(Group 2, non-infarction)

| Electrocardiogram grade | Fundal grade | | | | | Total |
|---|---|---|---|---|---|---|
| | I | II | III | IV | V+VI | |
| I+II (negative or doubtful) | 37 | 12 | 15 | 17 | 4 | 85 |
| III+IV (positive) | 4 | 2 | 5 | 6 | 10 | 27 |
| Total | 41 | 14 | 20 | 23 | 14 | 112 |

$p < 0 \cdot 001$ ($\chi^2 = 22 \cdot 54$ on 4 d.f.)

TABLE VII

DIASTOLIC BLOOD PRESSURE RELATED TO HYPERTENSIVE CHANGES IN ELECTROCARDIOGRAM
(Group 1, cardiac infarction)

| Diastolic blood pressure (mm. Hg) | Electrocardiogram grade | | | | Total |
|---|---|---|---|---|---|
| | I | II | III | IV | |
| <90 | 50 (72%) | 8 (50%) | 7 (41%) | 2 (20%) | 67 (60%) |
| >90 | 19 (28%) | 8 (50%) | 10 (59%) | 8 (80%) | 45 (40%) |
| Total | 69 | 16 | 17 | 10 | 112 |

$p < 0 \cdot 01$. ($\chi^2 = 13 \cdot 11$ on 2 d.f.) Grades III and IV considered as one for statistical treatment.

TABLE VIII

DIASTOLIC BLOOD PRESSURE RELATED TO HYPERTENSIVE CHANGES IN ELECTROCARDIOGRAM
(Group 2, non-infarction)

| Diastolic blood pressure (mm. Hg) | Electrocardiogram grade | | | | Total |
|---|---|---|---|---|---|
| | I | II | III | IV | |
| <90 | 49 (84%) | 16 (76%) | 10 (48%) | 0 (0%) | 75 |
| >90 | 9 (16%) | 5 (04%) | 11 (52%) | 8 (100%) | 33 |
| Total | 58 | 21 | 21 | 8 | 108 |

$p < 0 \cdot 001$ ($\chi^2 = 23 \cdot 33$ on 2 d.f.) Grades III and IV considered as one for statistical treatment.

(Table VI). This different experience in the infarct and non-infarct group is referred to in the discussion.

Electrocardiographic changes were also correlated with diastolic blood pressure (Tables VII and VIII). A significant relation was noted in both infarct and non-infarct groups in this case.

*Fundi and Heart Size.* Table IX records the relation between retinal artery changes and heart size in patients without infarction. The only significant difference in heart size exists between fundal grades I–IV and V+VI.

*Fundi and Thoracic Aortic Size.* Table X shows no significant correlation between retinal artery changes and the diameter of the thoracic aorta.

*Fundi and Previous History of Hypertension.* Table XI and Table XII show the association between retinal artery changes and a previous history

TABLE IX

RETINAL ARTERY CHANGES RELATED TO HEART SIZE
(Group 2, non-infarction)

| | Fundal grade | | | | | Total |
|---|---|---|---|---|---|---|
| | I | II | III | IV | V+VI | |
| No. of patients | 41 | 14 | 20 | 23 | 14 | 112 |
| Mean heart size | 47·54 | 46·41 | 48·85 | 46·87 | 51·43 | 47·95 |
| SD of mean | 5·55 | 3·86 | 5·39 | 5·85 | 6·87 | 5·70 |

Only significant difference here is between (I–IV) and (V+VI) ($0.05 > p > 0.01$) ($t = 2.19$ on 35 d.f.)

TABLE X

RETINAL ARTERY CHANGES RELATED TO AORTIC SIZE
(Group 2, non-infarction)

| | Fundal grade | | | | | Total |
|---|---|---|---|---|---|---|
| | I | II | III | IV | V+VI | |
| No. of subjects | 41 | 14 | 20 | 23 | 14 | 112 |
| Mean aortic size (mm.) | 58·83 | 54·93 | 60·00 | 59·70 | 61·86 | 59·11 |

TABLE XI

RETINAL ARTERY CHANGES RELATED TO PREVIOUS HISTORY OF HYPERTENSION
(Group 1, cardiac infarction)

| Previous history of hypertension | Fundal grade | | | | | Total |
|---|---|---|---|---|---|---|
| | I | II | III | IV | V+VI | |
| Positive | 3 (10%) | 5 (24%) | 7 (39%) | 7 (29%) | 9 (69%) | 31 (29%) |
| Negative | 28 (90%) | 17 (76%) | 11 (61%) | 17 (61%) | 4 (31%) | 77 (71%) |
| Total | 31 | 22 | 18 | 24 | 13 | 108 |

It was not possible to perform a significance test on these figures because of the small numbers in Groups V+VI.

TABLE XII

RETINAL ARTERY CHANGES RELATED TO PREVIOUS HISTORY OF HYPERTENSION
(Group 2, non-infarction)

| Previous history of hypertension | Fundal grade | | | | | Total |
|---|---|---|---|---|---|---|
| | I | II | III | IV | V+VI | |
| Positive | 3 (7%) | 0 (0%) | 6 (30%) | 9 (39%) | 9 (64%) | 27 (24%) |
| Negative | 38 (93%) | 14 (100%) | 14 (70%) | 14 (61%) | 5 (36%) | 85 (76%) |
| Total | 41 | 14 | 20 | 23 | 14 | 112 |

$p < 0.001$ ($\chi^2 = 26.33$ on 4 d.f.)

of hypertension in the infarct and non-infarct groups, respectively. The positive correlation in the infarct group is apparent and the correlation in the non-infarct groups is highly significant ($p < 0.001$). In addition, taking the 220 patients as one group, there is a clear association between retinal artery changes of hypertension and a previous history of treated or untreated high blood pressure.

A previous history of hypertension was also correlated with the diastolic blood pressure in the two groups of patients. Again, a highly significant correlation was noted (Tables XIII and XIV).

## COMMENT

These results show that, in patients with coronary heart disease, there is a clear correlation between the retinal artery changes of hypertension and the patients' systolic and diastolic blood pressure status, the electrocardiographic changes of hypertension and a previous history of hypertension. There appears to be a poorer correlation between retinal artery changes and heart size, and no correlation with the width of the thoracic aorta.

The correlation between retinal changes and systolic and diastolic blood pressure is clear in all our

TABLE XIII
PREVIOUS HISTORY OF HYPERTENSION RELATED TO DIASTOLIC BLOOD PRESSURE
(Group 1, cardiac infarction)

| Previous history of hypertension | Diastolic blood pressure (mm. Hg) | | Total |
|---|---|---|---|
| | < 90 | > 90 | |
| Positive | 12 (16%) | 19 (56%) | 31 (29%) |
| Negative | 62 (84%) | 15 (44%) | 77 (71%) |
| Total | 74 | 34 | 108 |

$p < 0{\cdot}001$ ($\chi^2 = 16{\cdot}03$ on 1 d.f.)

TABLE XIV
PREVIOUS HISTORY OF HYPERTENSION RELATED TO DIASTOLIC BLOOD PRESSURE
(Group 2, non-infarction)

| Previous history of hypertension | Diastolic blood pressure (mm. Hg) | | Total |
|---|---|---|---|
| | < 90 | > 90 | |
| Positive | 7 (10%) | 20 (47%) | 27 (24%) |
| Negative | 62 (90%) | 23 (53%) | 85 (76%) |
| Total | 69 | 43 | 112 |

$p < 0{\cdot}001$ ($\chi^2 = 17{\cdot}21$ on 1 d.f.)

patients, but these correlations are stronger and show a significant over-all trend from one fundal group to another only in the patients without infarction. Breslin *et al.* (1966) noted a positive correlation between diastolic blood pressure and retinal artery changes in patients without overt coronary heart disease.

It is our experience that accepted retinal arterial changes of hypertension, as expressed in our fundal groups V + VI, are highly suggestive evidence of previous as well as present hypertension, and must be considered strong indicators in this regard. This view is supported by the significant association between these advanced retinal changes and other hypertensive parameters such as electrocardiographic changes and a previous history of hypertension. In the 14 patients with well-established retinal artery changes (Grades V and VI) in the non-infarct group only one patient had a systolic blood pressure of less than 150 mm. Hg, and only 2 had a diastolic blood pressure of less than 90 mm. Hg.

The poorer correlation between retinal artery changes and systolic and diastolic blood pressure in the infarct group, particularly in regard to the over-all trend, must be considered as the effect of infarction on the patient's blood pressure status.

The much poorer correlation between retinal artery and electrocardiographic changes of hypertension in the infarct compared to the non-infarct group may be attributed to a number of causes, including the effects of infarction on QRS voltage and on the S–T changes of hypertension. Further, 50 per cent of the infarct group had diaphragmatic surface infarction, a topographical lesion that distorts the estimation of left axis deviation. It is clear, however, that electrocardiographic changes of hypertension as defined by us, if present, are a strong indication of previous hypertension, though the absence of such changes in patients with established infarction cannot be accepted as reliable negative evidence.

On the other hand, when the changes are correlated with the abnormal diastolic blood pressure of our patients, this correlation is if anything stronger in the infarct group. This apparently discordant finding requires further investigation and explanation.

Of particular interest was the usefulness of a positive previous history as an indicator of hypertension. Patients in both groups with a previous history of hypertension had a significantly higher diastolic blood pressure as well as a high frequency of hypertensive changes in the retinal arteries. It is apparent from this experience that a previous history of high blood pressure is important in assessing the blood pressure status of patients in a case-history study.

The heart size of our non-infarct patients tends to be greater in those with well-established retinal artery changes, but a normal heart size is a poor negative indicator of previous or present hypertension. However, obvious cardiomegaly in the absence of massive infarction with cardiac failure, and of other complicating factors, should alert the clinician to the likelihood of a hypertensive background.

The very poor correlation between aortic size and retinal artery changes was unexpected, but in our experience the measurement of the transverse aortic diameter proved particularly unreliable, largely because of the difficulty of defining the border of the ascending aorta. Clinical experience suggests useful association between thoracic aortic width and hypertension. It is possible, however, that the association may be less apparent in the younger age-groups under study. Our patients were all under 60 years.

## Conclusions

Assuming that the retinal artery changes of arteriovenous constriction, focal arterial narrowing, and fresh haemorrhages and exudates can be accepted as reliable indicators of past or present hypertension, and assuming that observer bias can be eliminated in measuring retinal artery changes, the following points emerge from this study.

The patient's contemporary systolic and diastolic blood pressure figures and electrocardiogram changes of hypertension are reliable indicators of previous hypertension, particularly in the non-infarct groups.

The presence of cardiac infarction reduces the reliability of contemporary systolic and diastolic blood pressure figures, and of electrocardiographic changes of hypertension.

Diffuse arterial narrowing or "silver wiring" should at least raise the suspicion of past or present hypertension.

A previous history of high blood pressure is useful confirmatory evidence of significant hypertension in the infarct and non-infarct groups.

Cardiomegaly, in the absence of cardiac failure or other causes, suggests the presence of past or present hypertension.

Measurement of thoracic aortic width is of little value in assessing blood pressure status.

## Summary

Hypertensive changes in the retinal arteries of 220 patients with coronary heart disease were correlated with other hypertensive parameters. These parameters included systolic and diastolic blood pressure; electrocardiographic changes of hypertension; previous history of hypertension; heart size and thoracic aortic width. High degrees of correlation were noted in the case of systolic and diastolic blood pressure, electrocardiographic changes of hypertension and a previous history of hypertension. Heart size correlated less well and aortic size correlated poorly. Patients with infarction tended to show a poorer correlation compared to patients who had not suffered an infarction.

This work, which is part of a case-history study of patients with coronary heart disease, aims to establish retrospectively the accurate pre-illness blood pressure status of patients with cardiac infarction.

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